

### REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated January 15, 2004.

The Examiner asserts that Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. and indicates that the application must contain a specific reference to the prior application(s) in the first sentence of the application. Applicants have above amended the specification to move the cross-reference, which is in the application as filed on lines 8-13, to the first sentence of the application.

### *Status of the Claims*

Claims 29-33 and 67-73 are pending in the application. Claims 32 and 33, which are withdrawn from consideration, have been canceled without prejudice. Claims 29, 30 and 31 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. In addition, Applicants have amended withdrawn claims 67, 68, 69, 70 and 73, which are withdrawn process claims, to include the limitations of the product claims. Applicants refer to the Examiner's comments in the Office Action at pages 3-4, stating that where Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Applicants request rejoiner of process claims including all the limitations of the product claims upon allowance of the product claims. Support for the amended claims can be found generally through Applicants' specification.

### *Claim Objections*

The Examiner objects to claims 29-31 as they encompass non-elected inventions and requests appropriate correction. Applicants have above amended claims 29-31 to remove the encompassed non-elected inventions, without prejudice.

The Examiner objects to claim 30 because it is not in sequence compliance. Applicants have above amended claim 30 to refer particularly to the hybrid truncated receptor polypeptide of amino acids 28-805 of SEQ ID NO: 10, as suggested by the Examiner. Applicants have

further above amended the specification to appropriately and consistently identify this hybrid receptor polypeptide. As stated by the Examiner at page 6 of the January 15, 2004 Office Action, Applicants assert and point out that this amendment does not constitute new matter.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's claim objections are obviated and should be withdrawn.

### ***The Double Patenting Rejection***

The Examiner has provisionally rejected claims 29-31 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 21, 22, 24, 26-28, 34-48, 51, 52 and 67 of copending Application Serial No. 08/599,974 ("the '974 Application"). Applicants respectfully disagree and submit that, in as much as the pending claims in the instant Application cover oligonucleotides hybridizable to OB-Re, these are patentably distinct from the nucleic acids coding on expression soluble leptin receptor OB-Re claimed in claims 21, 22, 24, 26-28, 34-48, 51, 52 and 67 of the copending '974 Application. However, in order to facilitate the conclusion of the prosecution of the instant application and as requested by the Examiner, Applicants submit herewith a Terminal Disclaimer to Obviate a Provisional Double Patenting Rejection Over A Pending Second Application with respect to the copending '974 Application.

### ***The 35 USC § 101 Rejection***

Claims 29-31 have been rejected under 35 U.S.C. 101 as directed to non-statutory subject matter. Applicants have above amended claims 29, 30 and 31 to refer particularly to "isolated" and assert that this rejection should now be properly withdrawn.

### ***The Specification Fully Enables the Claimed Invention***

Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that the claims as written include oligonucleotides

comprising fragments and homologues, and encompass oligonucleotides that vary substantially in length and also in nucleic acid composition. The Examiner states that the instant disclosure does not adequately support the scope of the claimed genus, under written description, which encompasses a substantial variety of subgenera. Applicants respectfully disagree and assert that Applicants have described and provided examples of soluble leptin receptors which support a genus claim. Applicants have described and provided the specific DNA and protein sequence for soluble receptor species OB-Re (SEQ ID NO:10) as well as the truncated variant of amino acids 28-805 of SEQ ID NO: 10. These species were isolated as a naturally occurring soluble receptor species, using procedures and methods detailed in the specification. The skilled artisan could readily, and without undue experimentation, isolate additional species of the genus of such soluble receptor(s), including additional and related allelic variants thereof.

In view of the foregoing remarks, Applicants submit that the Examiner's rejections under 35 U.S.C. 112, first paragraph may properly be withdrawn.

#### ***Particularity and Distinctiveness of the Claims***

The Examiner has rejected claims 29-31 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention.

The Examiner rejects claims 29-31 as indefinite because they encompass an oligonucleotide molecule hybridizable under "stringent" conditions. Applicants have above amended claims 29-31 to refer particularly to the hybridization and wash conditions.

In view of the foregoing remarks and amendments, Applicants request that the Examiner's rejections under 35 U.S.C. 112, second paragraph, be withdrawn.

#### ***The 35 USC § 102 Rejection***

Claims 29-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Tartaglia et al U.S. Patent No. 6,506,877, filed December 28, 1995. In particular, the Examiner states that Tartaglia et al. discloses a protein (SEQ ID NO: 2) that is 100% identical to amino acids 1-796 of SEQ ID NO: 10 of the instant invention and a nucleic acid (SEQ ID NO: 1) which is 98.9% identical to nucleotides 1-2443 of SEQ ID NO: 10. Applicants submit that Tartaglia et al. does

not anticipate the soluble leptin receptor of the instant invention and claimed by Applicants. Anticipation is a question of fact. As defined by the Federal Circuit, “[t]o anticipate a claim a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject-matter.” *PPG Industries, Inc. vs Guardian Industries Corp.*, 37 USPQ2d 1618 (Fed. Cir. 1996) (*emphasis added*). Tartaglia et al neither discloses every element of the rejected claims nor enables one skilled in the art to make the anticipating subject matter, specifically the soluble receptor of SEQ ID NO: 10 or the hybrid variant of SEQ ID NO: 10. SEQ ID NO: 2 of Tartaglia does not correspond to a soluble receptor, nor does it correspond in sequence to the soluble receptor(s) of the instant Application. As detailed in Tartaglia et al at page 6, lines 52-57, the deduced amino acid sequence (SEQ ID NO:2) of murine ObR protein has domains as follows:

signal sequence (amino acid residues 1 to about 22), extracellular domain (from about amino acid residue 23 to about 837), transmembrane domain (from about amino acid residue 838 to about 860), and cytoplasmic domain (from about amino acid residue 861 to 894).

SEQ ID NO: 2 and the SEQ ID NO: 1 encoding SEQ ID No: 2 of Tartaglia thus is not a soluble receptor and in fact includes a transmembrane and cytoplasmic domain. Applicants further point out that, as described in the instant specification, including at page 86, lines 28-30, soluble receptor OB-Re (SEQ ID NO:10) predicts a different amino acid sequence after His<sup>796</sup>. The Tartaglia sequence of SEQ ID NO:2 corresponds to SEQ ID NO: 10 up until His<sup>796</sup>, as indicated by Applicants, but does not teach or anticipate the unique C-terminal sequence of SEQ ID NO:10. Further, this C-terminal sequence after His<sup>796</sup> in Ob-Re is not even suggested by Tartaglia. In addition, Tartaglia describes an extracellular domain from about amino acid residue 837 and does not teach or anticipate, or even suggest, the end of natural DB sequence at amino acid His<sup>796</sup> in a soluble receptor form. Tartaglia et al. does not teach or anticipate the soluble receptor(s) as claimed by Applicants.

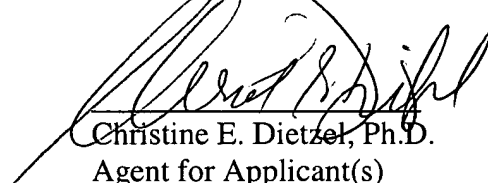
In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 102 may properly be withdrawn.

### CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

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**Complete Listing of Claims in Application U.S.S.N. 08/783,734**

Claims 1-28 (cancelled)

29. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule encoding on expression a soluble leptin receptor polypeptide selected from the group consisting of:

- a. a DNA molecule of SEQ ID NO:1, 3, 5, 7, or 9;
- b. a DNA molecule complementary to the DNA molecule defined in (a);
- c. a DNA molecule which is amplifiable ~~identifiable~~ with a polymerase chain reaction (PCR) probe selected from group consisting of a probe for clone 7 (forward primer SEQ ID NO:42 and reverse primer SEQ ID NO:43), a probe for clone 11 (forward primer SEQ ID NO:44 and reverse primer SEQ ID NO:45), and both clone 7 and clone 11; and
- d. a DNA molecule that codes on expression for the soluble leptin receptor polypeptide encoded by any of the foregoing DNA molecules.

30. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:

- a. a soluble leptin receptor selected from the group consisting of ~~OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Rc (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and OB-Re (SEQ ID NO:10),~~ or allelic variants thereof; and
- b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10, selected from the group consisting of:
  - i. ~~\_\_\_\_\_ N terminal corresponding to OB-Ra through Lys<sup>889</sup> and C terminal corresponding to a C terminal selected from the group consisting of OB-Rb after Lys<sup>889</sup> (SEQ ID NO:86), OB-Rc after Lys<sup>889</sup> (SEQ ID NO:87), and OB-Rd after Lys<sup>889</sup> (SEQ ID NO:88);~~
  - ii. ~~\_\_\_\_\_ N terminal corresponding to OB-Rb or OB-Rc through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra after Lys<sup>889</sup> (SEQ ID NO:89,90) or OB-Rd after Lys<sup>889</sup> (SEQ ID NO:91,92);~~
  - iii. ~~\_\_\_\_\_ N terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra after Lys<sup>889</sup> (SEQ ID NO:93), OB-Rb after Lys<sup>889</sup> (SEQ ID NO:94), or OB-Rc after Lys<sup>889</sup> (SEQ ID NO:95);~~
  - iv. ~~\_\_\_\_\_ N terminal corresponding to SEQ ID NO:84 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB-Ra after Lys<sup>889</sup> (SEQ ID NO:96), OB-Rb after Lys<sup>889</sup> (SEQ ID NO:97), OB-Rc after Lys<sup>889</sup> (SEQ ID NO:98), or OB-Rd after Lys<sup>889</sup> (SEQ ID NO:99);~~

v. ~~\_\_\_\_\_~~ N terminal corresponding to SEQ ID NO:84 from Met<sup>733</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB Ra after Lys<sup>889</sup> (SEQ ID NO:100), OB Rb after Lys<sup>889</sup> (SEQ ID NO:101), OB Re after Lys<sup>889</sup> (SEQ ID NO:102), or OB Rd after Lys<sup>889</sup> (SEQ ID NO:103);

vi. ~~\_\_\_\_\_~~ N terminal selected from the group consisting of OB Ra, OB Rb, OB Rd, and SEQ ID NO:84 from Pro<sup>664</sup> through His<sup>796</sup>, and OB Re from His<sup>796</sup> (SEQ ID NO:104,105,106 and 107); and

vii. ~~\_\_\_\_\_~~ N terminal corresponding to SEQ ID NO:84 from Met<sup>733</sup> to His<sup>796</sup>, and OB Re from His<sup>796</sup> (SEQ ID NO:108);

c. ~~\_\_\_\_\_~~ a leptin receptor wherein

i. ~~\_\_\_\_\_~~ the N terminal sequence is selected from the group consisting of

- ~~\_\_\_\_\_~~ (1) ~~\_\_\_\_\_~~ amino acid residues 1-889 (SEQ ID NO:109);
- ~~\_\_\_\_\_~~ (2) ~~\_\_\_\_\_~~ amino acid residues 23-889 (SEQ ID NO:110);
- ~~\_\_\_\_\_~~ (3) ~~\_\_\_\_\_~~ amino acid residues 28-889 (SEQ ID NO:111);
- ~~\_\_\_\_\_~~ (4) ~~\_\_\_\_\_~~ amino acid residues 133-889 (SEQ ID NO:112);
- ~~\_\_\_\_\_~~ (5) ~~\_\_\_\_\_~~ amino acid residues 733-889 (SEQ ID NO:113);
- ~~\_\_\_\_\_~~ (6) ~~\_\_\_\_\_~~ amino acid residues 1-796 (SEQ ID NO:114);
- ~~\_\_\_\_\_~~ (7) ~~\_\_\_\_\_~~ amino acid residues 23-796 (SEQ ID NO:115);
- ~~\_\_\_\_\_~~ (8) ~~\_\_\_\_\_~~ amino acid residues 28-796 (SEQ ID NO:116);
- ~~\_\_\_\_\_~~ (9) ~~\_\_\_\_\_~~ amino acid residues 28-796 preceded by an N terminal Asp-Pro dipeptide (SEQ ID NO:117);
- ~~\_\_\_\_\_~~ (10) ~~\_\_\_\_\_~~ amino acid residues 133-796 (SEQ ID NO:118); and
- ~~\_\_\_\_\_~~ (11) ~~\_\_\_\_\_~~ amino acid residues 733-796 (SEQ ID NO:119); and

ii. ~~\_\_\_\_\_~~ the C terminal sequence is selected from the group consisting of

- ~~\_\_\_\_\_~~ (1) ~~\_\_\_\_\_~~ SEQ ID NO:11;
- ~~\_\_\_\_\_~~ (2) ~~\_\_\_\_\_~~ SEQ ID NO:12;
- ~~\_\_\_\_\_~~ (3) ~~\_\_\_\_\_~~ SEQ ID NO:13;
- ~~\_\_\_\_\_~~ (4) ~~\_\_\_\_\_~~ SEQ ID NO:14; and
- ~~\_\_\_\_\_~~ (5) ~~\_\_\_\_\_~~ SEQ ID NO:15 after His<sup>796</sup> (SEQ ID NO:120);

d. ~~\_\_\_\_\_~~ a leptin receptor having an amino acid sequence selected from the group consisting of

i. ~~\_\_\_\_\_~~ Asp-Arg-Trp-Gly-Ser-Tyr<sup>420</sup> (SEQ ID NO:77) → Pro<sup>641</sup> (SEQ ID NO:121,122);

ii. ~~\_\_\_\_\_~~ Asp-Arg-Trp-Gly-Ser-Ser<sup>418</sup> (SEQ ID NO:78) → Pro<sup>641</sup> (SEQ ID NO:123,124);

iii. ~~Asp Arg Trp Gly Ser Leu<sup>123</sup> (SEQ ID NO:79) → Val<sup>331</sup> (SEQ ID NO:125,126); and~~

~~e. a leptin receptor as described in (a) (d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;~~

~~wherein the numbering is based on the amino acid sequence of SEQ ID :84.~~

31. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule having a nucleotide sequence corresponding or complementary to the DNA sequence set forth in SEQ ID NO:1, 3, 5, 7 or 9.

Claims 32- 66 (cancelled)

67. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:



- a. a leptin receptor selected from the group consisting of OB-Ra, OB-Rb, OB-Re, OB-Rd, and OB-Re (SEQ ID NO:10), or allelic variants thereof; and
- b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10, selected from the group consisting of:
  - i. N terminal corresponding to OB-Ra through Lys<sup>889</sup> and C terminal corresponding to a C terminal selected from the group consisting of OB-Rb, OB-Re, and OB-Rd after Lys<sup>889</sup>;
  - ii. N terminal corresponding to OB-Rb or OB-Re through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra or OB-Rd after Lys<sup>889</sup>;
  - iii. N terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, or OB-Re after Lys<sup>889</sup>;
  - iv. N terminal corresponding to SEQ ID NO:55 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys<sup>889</sup>;
  - v. N terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys<sup>889</sup>;
  - vi. N terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro<sup>664</sup> through His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and
  - vii. N terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and
- b. a leptin receptor wherein
  - i. the N terminal sequence is selected from the group consisting of
    - (1) amino acid residues 1-889;
    - (2) amino acid residues 23-889;
    - (3) amino acid residues 28-889;
    - (4) amino acid residues 133-889;
    - (5) amino acid residues 733-889;
    - (6) amino acid residues 1-796;
    - (7) amino acid residues 23-796;
    - (8) amino acid residues 28-796;
    - (9) amino acid residues 28-796 preceded by an N terminal Asp-Pro dipeptide;
    - (10) amino acid residues 133-796; and
    - (11) amino acid residues 733-796; and
  - ii. the C terminal sequence is selected from the group consisting of
    - (1) SEQ ID NO:11;
    - (2) SEQ ID NO:12;
    - (3) SEQ ID NO:13;
    - (4) SEQ ID NO:14; and
    - (5) SEQ ID NO:15 after His<sup>796</sup>;
- c. a leptin receptor having an amino acid sequence selected from the group consisting of
  - i. Asp-Arg-Trp-Gly-Ser-Tyr<sup>420</sup> (SEQ ID NO:77) > Pro<sup>641</sup>;
  - ii. Asp-Arg-Trp-Gly-Ser-Ser<sup>118</sup> (SEQ ID NO:78) > Pro<sup>641</sup>;
  - iii. Asp-Arg-Trp-Gly-Ser-Leu<sup>123</sup> (SEQ ID NO:79) > Val<sup>331</sup>; and
- d. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine; wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

68. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: ~~2, 4, 6, 8 and 10~~, or allelic variants thereof.

69. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

- a. a leptin receptor selected from the group consisting of ~~OB-Ra, OB-Rb, OB-Re, OB-Rd, and OB-Re (SEQ ID NO:10)~~, or allelic variants thereof; and
- b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10.  
selected from the group consisting of:

- i. ~~N terminal corresponding to OB-Ra through Lys<sup>889</sup> and C terminal corresponding to a C terminal selected from the group consisting of OB-Rb, OB-Re, and OB-Rd after Lys<sup>889</sup>;~~
- ii. ~~N terminal corresponding to OB-Rb or OB-Re through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra or OB-Rd after Lys<sup>889</sup>;~~
- iii. ~~N terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, or OB-Re after Lys<sup>889</sup>;~~
- iv. ~~N terminal corresponding to SEQ ID NO: 55 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys<sup>889</sup>;~~
- v. ~~N terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to Lys<sup>889</sup>, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys<sup>889</sup>;~~
- vi. ~~N terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro<sup>664</sup> through His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and N terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and~~

e. ~~a leptin receptor wherein~~

- ~~i. the N terminal sequence is selected from the group consisting of~~

- (1) ~~amino acid residues 1-889;~~
- (2) ~~amino acid residues 23-889;~~
- (3) ~~amino acid residues 28-889;~~
- (4) ~~amino acid residues 133-889;~~
- (5) ~~amino acid residues 733-889;~~
- (6) ~~amino acid residues 1-796;~~
- (7) ~~amino acid residues 23-796;~~
- (8) ~~amino acid residues 28-796;~~
- (9) ~~amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide;~~
- (10) ~~amino acid residues 133-796; and~~
- (11) ~~amino acid residues 733-796; and~~

- ii. ~~the C terminal sequence is selected from the group consisting of~~
- ~~(1) SEQ ID NO:11;~~
  - ~~(2) SEQ ID NO:12;~~
  - ~~(3) SEQ ID NO:13;~~
  - ~~(4) SEQ ID NO:14; and~~
  - ~~(5) SEQ ID NO:15 after His<sup>796</sup>;~~
- d. ~~a leptin receptor having an amino acid sequence selected from the group consisting of~~
- ~~i. Asp Arg Trp Gly Ser Tyr<sup>420</sup> (SEQ ID NO:77) → Pro<sup>641</sup>;~~
  - ~~ii. Asp Arg Trp Gly Ser Ser<sup>118</sup> (SEQ ID NO:78) → Pro<sup>641</sup>;~~
  - ~~iii. Asp Arg Trp Gly Ser Leu<sup>123</sup> (SEQ ID NO:79) → Val<sup>331</sup>; and~~
- e. ~~a leptin receptor as described in (a) (d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;~~
- ~~wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.~~

70. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with a oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8 and 10, or allelic variants thereof.

71. (withdrawn) The method of any of claims 67-70 wherein the oligonucleotide is labeled.

72. (withdrawn) The method of any of claims 67-70 wherein the nucleic acid molecule is RNA.

73. (withdrawn and currently amended) The method of any of claims 67-70 wherein the oligonucleotide is selected from the group consisting of SEQ ID NO: 20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, ~~SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54.~~